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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/620,787	07/15/2003	John Simard	51300-00006	1118

45200 7590 04/14/2006

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EXAMINER	
HURT, SHARON L	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 04/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/620,787	SIMARD ET AL.	
	Examiner	Art Unit	
	Sharon Hurt	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *3-6 and 12-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7-11 and 18-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-2, 7-11 and 18-26, in the reply filed on March 22, 2006 is acknowledged. The traversal is on the ground(s) that Groups I and II are both classified in the same class and subclass therefore, a separate search is not required and that the subject matter is linked by a common concept. Applicant's argument is found persuasive; therefore **Group II**, claims 1-2, 7-11 and 18-26, drawn to vaccinia virus will also be examined on the merits.

Applicant's election with traverse of Group A, M1R protein, in the reply filed on March 22, 2006 is acknowledged. The traversal is on the ground(s) that a polyprotein requires "more than one protein" therefore restriction to one protein is inappropriate. Applicant's argument is found persuasive and the restriction to elect one protein in Groups A-L has been **withdrawn**.

Claims 3-6 and 12-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on March 22, 2006. Claims 1-2, 7-11 and 18-26 are under consideration.

Claim Objections

Claims 18 and 19 are objected to because of the following informalities: The claims contain reference to nonelected claims which have been withdrawn from consideration. Appropriate correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention7 CFR 1.821(d) requires the use of the assigned sequence identifier (SEQ ID NO:) in all instances where the description of a patent application refers to a sequence and whenever a sequence or fragment thereof is claimed (see MPEP 2422.03).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Moyer et al (US Patent No. 5,212,057).

Claim 20 is drawn to an immunogenic composition comprising a complex of polypeptides wherein each polypeptide comprises an external immunogen of a membrane-associated protein of variola major or vaccinia virus.

Moyer et al. teaches a vaccine construct comprising any avirulent poxvirus modified by insertion of a marker gene from a different poxvirus (see column 4, lines 8-49). Moyer et al. teach recovery of recombinant viral progeny, which would comprise a complex of polypeptides comprising external immunogens of cross-reactive polypeptides. Therefore, Moyer et al. anticipates the invention of claim 20.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 7-11 and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent Application No. 09/781,124 (Hooper et al.) and Thomson et al., (The Journal of Immunology, 1998, Vol. 160, pages 1717-1723).

The claimed invention is drawn to a polyprotein comprising external immunogens of membrane-associated proteins of variola major or vaccinia virus; wherein at least two of the poxvirus membrane-associated proteins are selected from the group consisting of: M1R, A36R, I5R, B7R, F8L, A30L, A33R, H5R, B5R, D8L, and A27L; wherein the antibodies against one of the proteins are synergistic with antibodies against one other protein; wherein the synergistic antibodies recognize A36R of variola major or A33R of vaccinia; wherein the immunogen or cocktail of immunogens is made according to the method listed; wherein an immunogenic composition comprising a complex of polypeptides wherein each polypeptide comprises an external immunogen of a membrane-associated protein of variola major or vaccinia virus; wherein the polypeptides are biotinylated and the complex is formed by the addition of avidin or strepavidin or the complex is formed by anchoring the polypeptides in a liposome or micelle; wherein the polyprotein comprising external immunogens of membrane-associated proteins of variola major wherein the individual proteins are joined through a linker-spacer peptide, having the sequence GGGGSSGG; further comprising an affinity tag wherein the affinity tag is a poly-histidine tag.

Hooper et al. teaches about vaccinia virus and variola virus and a live virus vaccine to prevent disease (paragraphs 002-003). Hooper teaches a composition of one or more vaccinia antigens which are used to elicit antibodies in mice and are defined to be important for protection (paragraph 005). Hooper teaches that one neutralizing monoclonal antibody alone, i.e. antibodies raised against proteins D8L or A27L, did not provide protection and that antibodies against two or more proteins, i.e.

L1R and A33R, are required for protection (paragraphs 006-007). Hooper et all also teach that L1R and A33R homologs from other poxvirus can be used as immunogens to produce monoclonal antibodies, which would most likely be protective since homologs in other poxviruses have high identity with the vaccinia virus proteins (paragraph 009). Therefore these surface proteins are synergistic with antibodies against at least one other protein. Hooper teaches that monoclonal antibodies raised against L1R and A33R protect against vaccinia virus infection (paragraph 0009). Hooper further teaches monoclonal antibodies raised against vaccinia antigens L1R, A33R, H3L, D8L, A27L and A17L (paragraph 0023). Hooper does not teach construction of a single polyprotein comprising two or more proteins of variola major or vaccinia virus.

Thomson et al. teaches delivery of multiple epitopes by DNA vaccination. Thomson describes a DNA plasmid encoding a polyepitope protein, which contains multiple murine epitopes. Mice vaccinated with this plasmid made cytotoxic T cell (CTL) responses to each of the epitopes and protective CTL, were demonstrated in recombinant vaccinia virus. Thomson teaches the ability to deliver large numbers of CTL epitopes using relatively small polyepitope constructs and that DNA vaccination technology should find application in the design of human epitope-based CTL vaccines (page 1717 Abstract).

One of ordinary skill in the art at the time the invention was made would have found it *prima facie* obvious to have consolidated the membrane associated proteins taught by Hooper into a single polyprotein, as taught by Thomson, as an effective

means of delivering multiple antigens of variola major or vaccinia virus in order to elicit a protective immune response.

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hooper et al. in view of Thomson et al., as applied to claims 1-2, 7-11 and 18-20 above, and further in view of Curiel et al. (US Patent No. 6,274,322).

The claimed invention is drawn to an immunogenic composition comprising immunogenic polyproteins of variola major and/or vaccinia wherein the proteins are complexed with biotin and avidin or streptavidin.

Hooper et al. in view of Curiel et al. teach immunogenic polyproteins comprising proteins of variola major and/or vaccinia, as described above. Neither Hooper et al. nor Thomson et al. teach that the polypeptides are biotinylated or teach formation of a complex via avidin or strepavidin binding.

Curiel et al. teaches conjugates which contain a virus, wherein binding of the virus is through a biotin-streptavidin bridge (column 17, lines 12-17). Curiel teaches that complexes consisting of DNA and streptavidin-protein, to which the biotin modified virus is bound, have a high transfection efficiency, even at lower concentrations of DNA. Curiel also notes that the binding to biotin may also be effected by means of avidin.

One of skill in the art at the time the invention was made would have found it *prima facie* obvious to have used a biotin-strepavidin bridge to make a conjugate of proteins from variola major and/or vaccinia because Curiel et al teach a high transfection efficiency when proteins are conjugated via biotin-avidin.

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hooper et al. in view of Thomson et al., as applied to claims 1-2, 7-11 and 18-20 above, and further in view of Rutter et al (US Patent Application Publication No: US 2002/0015707 A1).

The claimed invention is drawn to an immunogenic composition comprising immunogenic polyproteins of variola major and/or vaccinia wherein the proteins are anchored in a liposome or micelle.

Hooper et al. in view of Thomson et al. teach immunogenic compositions comprising proteins of variola major and/or vaccinia as set forth *supra*. Neither Hooper et al. nor Thomson et al. teach anchoring the proteins in a liposome or micelle.

Rutter et al. teaches a nucleic acid vaccine comprising an agent to facilitate delivery of the vaccine wherein the agent is a liposome (paragraph 037 and 040).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have anchored the proteins of Hooper in view of Thomson in a liposome, as taught by Rutter et al., in order to facilitate delivery of the proteins.

Claims 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hooper et al. in view of Thomson et al., as applied to claims 1-2, 7-11 and 18-20 above, and further in view of Newton et al., (Biochemistry, 1996, Vol. 35, pages 545-553).

The claimed invention is drawn to an immunogenic composition comprising immunogenic polyproteins of variola major and/or vaccinia wherein the proteins are joined through a linker peptide (specifically GGGGSSGG) and wherein the polyprotein further comprises an affinity tag (or specifically a poly-histidine tag).

Hooper et al. in view of Thomson et al. teach immunogenic compositions comprising proteins of variola major and/or vaccinia as set forth *supra*. Neither Hooper et al. nor Thomson et al. teach joining the proteins together with a linker or attaching an affinity tag. Newton teaches flexible peptide linkers used to join fusion proteins as Gly-Ser linkers $(GGGGS)_3$ (page 545, Abstract). Newton also teaches attaching a poly-histidine affinity tag to facilitate purification of the fusion proteins (page 546, second column).

One of ordinary skill in the art at the time the invention was made would have found it *prima facie* obvious to have used a flexible linker peptide (Gly-Ser) coding sequence as taught by Newton as an effective means of joining polypeptides together and to have used the poly-histidine tag taught by Newton as an effective means to facilitate purification of the polyproteins.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Roper et al. (Journal of Virology, June 1996, Vol. 70, No. 6, pages 3753-3762) and US Patent Application Publication No: US 2002/0028219 A1 (Smyth-Templeton et al.).

Roper et al. teaches that A33R is a glycoprotein localized in the outer envelope of vaccinia virus.

Smyth-Templeton et al. teaches highly efficient cationic as an improved delivery system for biologically active reagents.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon Hurt whose telephone number is 571-272-3334. The examiner can normally be reached on M-F 8:00 - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Housel James can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharon Hurt

April 12, 2006

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